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Joan Claybrook, President

April 28, 2000

Charles Gaylord
Office of International and Constituent Relations (HFG-1)
Food and Drug Administration
5600 Fishers Lane
Rockville MD 20857

Re: Docket Number 98S1064

Dear Mr. Gaylord,

On December 8, 1999, the Food and Drug Administration (FDA) held a public meeting to discuss the progress in implementing the Pharmaceutical GMP (Good Manufacturing Practices) Annex of the Agreement on Mutual Recognition (MRA) between the U.S. and the European Community. This letter expands upon concerns Public Citizen raised at the meeting.

The purpose of the GMP Annex is to permit foreign drug regulatory authorities to conduct GMP inspections in their nations on behalf of the FDA. To achieve this goal, the U.S. will examine the Pharmaceutical GMP regulatory systems of each of the E.U. member nations to determine whether or not each is "equivalent" to the U.S. regulatory system.

The GMP Annex defines equivalence as involving "systems [that] are sufficiently comparable to assure that the process of inspection and the ensuing inspection reports will provide adequate information to determine whether respective statutory and regulatory requirements of the authorities have been fulfilled. Equivalence does not require that the respective regulatory systems have identical procedures." Several FDA representatives at the December meeting stressed that the agreement did not mean that standards would be harmonized. However, in response to an audience question, Joseph Famulare of the FDA's Center for Drug Evaluation and Research responded, "There is certainly no prohibition against certain harmonizations taking place. I think it's just a natural outcome of the process."

Recommendation: Given these contradictory statements, the FDA should clarify whether and what harmonized standards are likely to result from the MRA. If indeed harmonization of standards is contemplated, FDA should plainly state the process it will use to incorporate public comment into the harmonization process. Public Citizen reminds the FDA that any change of any U.S. standard or adoption of a foreign standard, must be accompanied by notice and comment rulemaking.

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Next, with regard to the pending equivalence determinations, Public Citizen rejects the notion of equivalence propagated by the North American Free Trade Agreement and World Trade Organization agreements. The very notion of equivalence allows for imprecise, subjective comparisons that are not appropriate when dealing with issues as important as public health and safety. However, given that equivalency decisions between nations are moving forward, we urge exacting criteria for making equivalence determinations. A standard or a regulatory system should only be declared equivalent if it provides precisely the same or greater level of substantive protection for public health and safety and after there is an appropriate opportunity for public comment.

In the case of the GMP Annex, the criteria identified in Appendix 4 of the MRA provide no assurance that determinations of equivalence will result in the same level of public safety for U.S. consumers. Rather, the criteria are strikingly vague and seem designed to assure maximum flexibility to facilitate a determination of equivalence. In the absence of specific criteria, any determination of equivalence will be meaningless from a public health standpoint.

Rather than discussing each of the criteria, we will review three examples. First, the criteria include "Authority to make inspections, review and copy documents and to make samples and collect other evidence." There can be little question that many (if not all) regulatory bodies in Europe have such authority, but the real question is: Do they actually make these inspections? Rather than requiring "authority" for equivalence, there should be specific quantitative criteria that must be met: numbers of inspections per unit time, percentage of facilities inspected per unit time, length of inspections, numbers of inspectors per facility, etc. Moreover, there needs to be greater assurance that these inspections are of equivalent stringency: Do similar infractions receive similar penalties?

Second, the criteria also include "Mechanisms in place to assure appropriate professional standards and avoidance of conflict of interest." While we certainly agree that these are relevant criteria, they must be broken down into their basic elements and each of these must be assured. How will conflict of interest be avoided? What specific mechanisms do the European countries have to avoid conflict of interest, and how do they compare with our own? What is the nation's track record on enforcement? Without a detailed comparison of specific conflict of interest standards and enforcement histories, the criteria are meaningless.

A third and final example concerns "accountability of the regulatory authority." This phrase, like the two above, is so nebulous as to be devoid of meaning. From Public Citizen's perspective, an accountable regulatory authority is one that, at a minimum, has Freedom of Information standards no weaker than our own, has provisions for notice and comment rulemaking equivalent to our own, announces and then holds advisory committee meetings in public, and can be challenged in court, on either procedural or substantive grounds. Again, FDA must flesh out the details and assure that there is equivalence for each of these "sub-criteria" or else any determination of equivalence will not be credible.

The FDA is planning to examine the equivalency of each country on a case-by-case basis over the course of the next two years or more. However, at the December 8th meeting, in response to a question on whether or not the FDA will notice a pending equivalency decision as a proposed rule, the FDA indicated that it did not think further notice was necessary, but that it would maintain an open docket. It appears that the FDA believes the November 6, 1998 (63 FR 60121) notice of the MRA as a whole is sufficient public notification for these equivalency decisions.

In contrast, the FDA's detailed procedure for determining equivalence in the food safety area (62 FR 30593, June 4, 1997) calls for a preliminary determination of whether equivalence exists for each particular country followed by notice and comment rulemaking. The FDA will not issue a final determination on the issue of equivalence without taking into account the comments received.

> **Recommendation:** The FDA can greatly increase public confidence in the MRA equivalency process with early notice and comment rulemaking on each proposed equivalency decision. Such notices must lay out, in detail, the case for equivalency and must clearly identify all the sub-criteria examined, any aspect of the other nation's regulatory system that differs from the U.S. system, and why the FDA believes that system affords an equivalent level of public protection. The FDA should respond to comments and concerns by the public on the record, before making a final equivalency determination.

At the December 8th meeting, the FDA indicated that if a determination of equivalence is made in a closed Joint Sectoral Committee meeting, the FDA will notify the public of its final decision via the Federal Register and give its reasoning for the decision. This is, of course, too late for meaningful public input. Moreover, if an equivalency determination is not made, the FDA will not notify the U.S. public, but will let the requesting country know about any problem areas the FDA has identified. Thus the public will be unaware of what problems were identified and will be unable to comment on those problems or measure progress on ameliorating the problems. While predecisional data regarding confidential business information are restricted in certain circumstances, it is illogical that information regarding another nation's system of laws, regulations and enforcement history is being treated in the same manner.

Examining the equivalency of each nation's regulatory system is a massive endeavor that will entail an enormous expenditure of public resources. The GAO estimated that the FDA will need $10 million for 125 full time staff and other expenses to reach the first year of the MRA's implementation stage. Public Citizen wants to make sure that interested consumers and taxpayers enjoy the fruits of these investigations and analysis.

Recommendation: The FDA should make predecisional information concerning any equivalence determination available to the public prior to a final determination and allow for notice and comment. At the very latest, this information should be released at the time an equivalence decision is made, pro or con.

Finally, we are concerned about which documents currently available to the U.S. public under the Freedom of Information Act would remain available after the FDA's inspection duties are turned over to regulators of other nations.

Recommendation: The FDA should affirm that the following U.S. documents will continue to be made available to the public when the MRA is fully implemented and the documents are generated by regulatory authorities of other nations: 1) inspection reports (including 483s); 2) enforcement reports (bi-weekly list of recalls); 3) notices of violation; and 4) warning letters. For a foreign drug regulatory authority to be deemed equivalent to the FDA, there must be a guarantee that the foreign equivalents of these documents are also available. The FDA should also make plain the process by which U.S. citizens will gain access to these foreign documents.

The Joint Sectoral Committee will determine which regulatory authorities are ready to be deemed "equivalent." The Joint Sectoral Committee is made up of representatives from the FDA and the European Commission who have responsibility for pharmaceutical GMPs. Each government has one vote on any equivalency decision, and all decisions are made by unanimous consent. Joint Sectoral Committee meetings will be closed to the public.

The events in Seattle at the end of November demonstrate that the U.S. public is fed up with the undemocratic and non-transparent manner in which the U.S. government conducts its trade policy. It is contrary to the culture of open and accountable governance touted by the FDA at the December 8th meeting to allow final decisions about equivalence to be reached behind closed doors.

Recommendation: Public Citizen asks that the meetings of the Joint Sectoral Committee and the Joint Committee, which may be involved in resolving disputes regarding equivalency, be open to public observation and transcripts of all committee business be posted on the websites of the FDA and the Office of the U.S. Trade Representative.

Attached please find a paper produced by the Transatlantic Consumer Dialogue (of which Public Citizen is a member) called *Principles of International Harmonization*. The TACD is comprised of 65 consumer groups on both sides of the Atlantic representing some 600 million consumers. The paper outlines consumer concerns with international harmonization, equivalency

and Mutual Recognition Agreements. We hope the paper will be taken into consideration by the FDA as it moves forward with the implementation of the U.S.-E.U. MRA.

Sincerely,

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TACD

TRANS ATLANTIC CONSUMER DIALOGUE

DIALOGUE TRANSATLANTIQUE DES CONSOMMATEURS

DOC NO. TRADE-8-00

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PRINCIPLES OF HARMONIZATION

International harmonization can occur at the lowest or highest level of public health, worker safety, or environmental protection. However, the TACD strongly believes that in the instances when international harmonization of standards is appropriate, it must result in the adoption of best available technology and embody the highest levels of consumer protection. Unfortunately, the actual provisions of the WTO requiring harmonization or providing incentives for harmonization generally promote the lowering of the best existing domestic public health, food safety, economic justice, natural resource conservation and product safety standards. For instance, under the WTO, international standards do not serve as a floor that all countries must meet. Rather, they serve as a ceiling. The agreements provide for the challenge of any domestic standards that go beyond international standards in providing greater citizen safeguards, but contain no provisions for challenging lax standards. Thus, as outlined in its position paper in preparation for the Seattle Ministerial, the TACD is concerned that as currently written, the permanent WTO agreements and provisions will serve only as a one-way downward ratchet on domestic standards. In the wake of Seattle, TACD affirms that the review and repair of the WTO's Technical Barrier to Trade Agreement and the Sanitary and Phytosanitary Agreement is an urgent priority that is more attainable than ever.

Principles for International Harmonization:

1. **Standards that do not have a health and safety component should be the primary candidates for international harmonization.** We must distinguish between standards and procedures that do not directly involve health and safety concerns (i.e. the size of a floppy disk, credit card, or customs and accounting procedures) and those that impact health and safety (i.e. auto standards, medical device standards, and allowable pesticide residues in food.). Many standards, like pesticide residues, are impacted by factors such as cultural norms, dietary intake which make a "one size fits all" standard hard to achieve.

2. **Some issues must remain outside the scope of international commercial rules altogether.** We reject the movement fostered in the WTO to turn basic necessities or elements of life (like genetic materials) into commodities. Rather they should be recognized as common goods and precious resources for government to protect, distribute and regulate. For example, we reject the commodification of bulk water, and the patenting of life forms and seeds.

3. **TACD favors international standards being used as a floor rather than a ceiling.** The harmonization mechanisms in the TBT and SPS Agreements encourage the challenge of higher domestic standards but not the challenge of lower standards. The current mechanism

can only result in a ratcheting down of standards. At a minimum, the harmonization provisions of the SPS and TBT agreements need to be rewritten to ensure that the role of democratically-achieved international standards is not to discourage cutting-edge domestic innovations geared toward solving some of our most pressing problems.

4. **TACD is concerned about current WTO use of international standards in deciding disputes regarding health, safety and the environment**. TACD believes that international standards, while helpful in some contexts, should be voluntary and that the WTO SPS and TBT Agreements' current elevation of all such standards, regardless of the forum in which they are set or the level of protection provide, is inappropriate. For instance, international standards should not be used to undermine non-discriminatory domestic standards merely because those domestic standards provide a higher level of health, safety or environmental protection. TACD is particularly concerned at the practical application of international standards in the dispute resolution procedure. Not enough emphasis is being placed on the exception which allows nation states to adopt higher standards or requirements. This is compounded by the inability to challenge international standards themselves for not embodying a sufficiently high level of consumer protection.

5. **The Precautionary Principle should be incorporated more broadly in the international standards setting process**. Ironically, while the U.S. government challenges the EU beef hormone and genetically modified organisms (GMO) policies at the WTO, it undercuts the underlying basis for regulatory policy in the U.S. For example, the FDA's pharmaceutical safety rules, the burden of proof is on the producer to show a drug is safe. Until there is scientific evidence to make that showing, the drug is kept off the market. If a precautionary approach had been systematically applied, it might have prevented some of the recent and deadly food safety crises in Europe. Bringing such a principle to life is merely a matter of setting the right rules. The obvious test as to a standard's trade effect -- and the one that would have safeguarded the beef hormone policy -- is whether the measure is discriminatory as between domestic and foreign goods. The rule we demand is that standards based on the Precautionary Principle and applied equally to domestic and foreign producers are inherently permissible.

6. **Governments should only recognize or be involved in harmonization activities negotiated in open, accountable democratic fora**, with clear avenues for public input and transparent methods of rulemaking and record keeping. Non-transparent private industry groups for example, are not the place to be setting WTO-presumptively legal standards which impact public health, consumer safety or the environment. If differing regional and international standards are to be harmonized then this should take place within an open and transparent framework. This framework must allow for participation by consumer representatives at all levels and all stages of the standards-writing process. Greater co-operation between government officials is also required to agree on essential safety requirements, which should be applied to international standards. Provision should also be made for public and/or government review and possible challenge of the right of a particular international standard to give any presumption of compliance with legal requirements. Other, quasi-governmental organizations like the Codex Alimentarius must also be reformed to give consumers and equal voice with industry in the process.

7. **a. We reject the notion of functional equivalence**. In Europe, equivalency decisions have been a conspicuous failure that has eventually resulted in the writing of over 5,000 new European standards with some 8,000 more on the way. Standards provide a bright line test whereby precise comparisons can be made. The very notion of equivalence allows for imprecise, subjective comparisons that are not appropriate when dealing with issues as important as public health and safety. However, given that equivalency decision between nations are moving forward with increasing frequency, we must develop strict rules for making equivalence determinations. A standard or a regulatory system should be determined equivalent only if it provides the same or greater level of substantive protection for health, safety or the environment. Criteria for determining equivalency should be clearly outlined and equivalency proposals should have substantive public input before they reached. (Thus, the NAFTA equivalence finding on Canadian beef that did not even review, much less compare, the varying regulatory systems and numerous standards, is unacceptable.)

   b. Any equivalence decision or Multilateral Recognition Agreement (MRA) must ensure that the procedural safeguards of the countries involved are equally strong -- meaning there is a democratic process that assures consumer input and redress and government enforcement. To this end we recommend readiness criteria under which potential MRA and equivalency agreement must be reviewed. We urge nations to adopt strong freedom of information provisions, on-the-record rulemaking procedures, laws providing for open meetings of governmental agencies and balance on advisory committees among other reform measures to encourage citizen input into trade-related and standards-related proceedings.

8. **Harmonization activities including MRAs and equivalency agreements are only ever appropriate if they enhance the well-being of the people of the nations involved**. If these agreements are not negotiated with the input of the citizenry and if there is not a clearly defined public benefit, there is no reason for governments to spend public resources to accomplish harmonization. The cost of harmonization which only benefits industry should be shifted back to the private sector to execute voluntary standards. (For example, the FDA estimates that the 1998 U.S.-EU MRA will cost them over $10 million and 125 full-time employees to implement.)

9. **We oppose the TABD's call for increased reliance on "suppliers declaration of conformity**," especially in sensitive areas including: public health, food, product and worker safety and the environment. Conformity assessment procedures are only one component of the framework which ensures that products actually comply with the appropriate standards. This framework includes the product liability regime and market surveillance in particular. The role that each of these components will play can legitimately differ from one jurisdiction to another. There is a danger that focussing on only one aspect i.e. conformity assessment will upset the balance of the whole framework. Some equivalency decisions and MRAs (i.e., 1998 U.S.-EU MRA) are leading to situations where one country is handing over federal regulatory authority to private entities in a second country. TACD believes it is entirely inappropriate to privatize key public safety functions via MRAs and equivalency decisions, even if national governments retain ultimate responsibility for the safety of products.